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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,945	11/01/2001	Gary L. Olson	PPI-106CP2	9920

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT

PAPER NUMBER

1654

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/001,945	Applicant(s) OLSON ET AL.	
	Examiner. Jeffrey E. Russel	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-65 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-65 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

*S.02*

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1. Applicant's election with traverse of the peptide of SEQ ID NO:16 in the reply filed on December 16, 2004 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

This application contains claims 47 and 55 reciting amino acid sequences nonelected with traverse in the reply filed December 16, 2004. A complete reply to the final rejection must include cancellation of nonelected amino acid sequences or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

2. The following errors in amendment format with respect to the amendment filed June 20, 2005 are noted: In the amendment to the paragraph at page 15, lines 3-13, second-to-last line of the paragraph, "pyridylpropionic" was changed to "pyriylpropionic" without the change being marked as required by 37 CFR 1.121(b)(ii). In the amendment to Table IV at page 61 of the specification, in the entry for Example 16, "proprionic" was changed to "propionic" without marking. In amended claim 19, last group shown in the claim, a methyl group was added to the non-cyclic nitrogen atom without the change being marked as required by 37 CFR 1.121(c)(2). In amended claim 40, formulas (IV) and (V), "CH<sub>3</sub>" was deleted from the right-hand side of each formula without the changes being marked. In amended claim 40, line 5, "Wherein" was changed to "wherein" without the change being marked. In amended claims 41 and 48, a CH<sub>3</sub> group was deleted from the oxiranyl group without marking. In amended claim 41, two occurrences of "CH<sub>3</sub>" were deleted from the right-hand side of the formula without marking. Any future amendments should be carefully reviewed to ensure full compliance with the amendment format rules.

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3. The priority claim contained in the amendment filed June 20, 2005 is objected to because the application serial number and filing date for grandparent application 09/704,251 need to be re-inserted so that standard priority claim language is used. Correction is required.

4. The disclosure is objected to because of the following informalities: In the amended paragraph at page 15, lines 3-13, the sequence designated "SEQ ID NO:30" does not correspond to SEQ ID NO:30 as defined in the sequence listing filed June 17, 2003. In the amended paragraph at page 15, lines 3-13, second-to-last line of the paragraph, "pyridylpropionic" is misspelled. In Table IV at page 61, the amended amino acid sequence given for Example 14/ID#30 does not correspond to the structural formula given for Example 14 at page 51.

Appropriate correction is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 41 and 48-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 41 and 48 have been amended so that the oxiranyl group is no longer methyl-substituted. There is no original disclosure of a MetAP-2 inhibitory core having this particular structure. There is no original disclosure of the compound recited at claim 57, page 16, lines 15-16. It appears that this compound may have been intended to be a corrected version of the originally-filed compound which included "ID#40" in its name. However, there never was

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a SEQ ID NO:40 in any sequence listing in the application, and in corresponding Example 16, there is no Asp residue. There is no original disclosure of the compound recited at claim 57, page 17, lines 1-2. The peptide portion of this compound, Ac-ProLeuMetTrpAla, is not disclosed in the sequence listing or in any of the tables or examples of the specification. There is no original disclosure of the compound recited at claim 57, page 17, lines 3-4. The peptide portion of this compound, Ac-ProLeuGlyMet, is not disclosed in the sequence listing or in any of the tables or examples of the specification.

6. Claims 1-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. At claim 1, in formula I and at lines 6 and 9-12, and in the last two lines, the same variable names  $R_2$  and  $R_3$  are used to designate different substituents of the compound and are defined differently from one another. This makes it unclear, e.g., as to which substituents are being further limited in dependent claims 2-6. The independent claim should be re-written so that different variable names are used for the differently-defined substituents. For analogous reasons, independent claim 20 and dependent claims 34-41 are also indefinite because they use the same variable names  $R_2$  and  $R_3$  to designate different substituents of the same compound, and define these variable names differently depending upon the substituent. The claims should be re-written so that different variable names are used for the differently-defined substituents.

7. Claims 23, 24, 28, 29, 49, 50, and 57 are objected to because of the following informalities: The provided clauses inserted into claims 23 and 28 appear to be redundant because the claims do not permit Q to be hydrogen under any circumstances. The redundant provided clause should be deleted from each claim. The provided clause inserted into claim 49

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appears to be redundant because the claim does not permit P to be hydrogen, NHR or OR under any circumstances. The redundant provided clause should be deleted from the claim. At claim 57, page 16, lines 9-16 and 19-20, and page 17, lines 1-6, SEQ ID NOS corresponding to the recited amino acid sequences must be inserted after each of the compound names. See 37 CFR 1.821(d). At claim 57, page 16, line 19, "Carbamoyl" is misspelled. Appropriate correction is required.

8. Claims 2-6 and 41 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Independent claim 1 has been amended so that R<sub>3</sub> and R<sub>4</sub>, if they are alkyl or aryl groups, are required to be substituted alkyl or substituted aryl groups. However, dependent claims 2-6 still permit R<sub>3</sub> and R<sub>4</sub> to be unsubstituted alkyl groups, unsubstituted aryl groups, or phenyl, naphthyl, benzyl, or naphthylmethyl groups. Accordingly, dependent claims 2-6 embrace groups which are not embraced by the independent claims, and are therefore improper dependent claims. Claim 41 has been amended so that the oxiranyl group is no longer methyl-substituted. Accordingly, the A group of claim 41 is no longer a species of one of the A groups set forth in claim 40, upon which claim 40 depends.

9. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The

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filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

10. Claims 23, 24, and 58-61 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 4, 5, 9, 10, 30, 31, and 39-42 of prior U.S. Patent No. 6,548,477. This is a double patenting rejection.

11. Claims 21-24 and 58-61 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 21-24 and 58-61 of copending Application No. 10/429,174.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 2-6, 20-22, 25-40, 42-47, and 62-65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-52 of U.S. Patent No. 6,548,477. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '477 patent anticipate the instant claims.

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14. Claims 2-6, 20-40, 42-47, and 58-65 are directed to an invention not patentably distinct from claims 1-52 of commonly assigned U.S. Patent No. 6,548,477. Specifically, see the obviousness-type double patenting rejection set forth in section 13 above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302).

Commonly assigned U.S. Patent No. 6,548,477, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

15. Claims 1-40, 42-47, 57-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-73 of copending Application No. 10/429,174. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '174 application clearly anticipate the instant claims.



This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 2-6, 20-40, 42-47, and 58-65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-43, 45-48, and 50-61 of copending Application No. 09/972,772. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '772 application anticipate the instant claims. Note that a composition comprising a compound anticipates claims drawn to the compound per se.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 2-6, 20-40, 42-47, and 58-65 are directed to an invention not patentably distinct from claims 1-52 of commonly assigned copending Application No. 09/972,772. Specifically, see the obviousness-type double patenting rejection set forth in section 16 above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302).

Commonly assigned copending Application No. 09/972,772, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

18. Claims 2-6, 20-40, 42-47, 57, 58, 61, 62, and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-53 of U.S. Patent No. 6,919,307 (which issued based upon Application No. 10/138,935). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '307 patent anticipate the instant claims. Note that a process of using a compound anticipates claims drawn to the compound per se.

19. Claims 2-6, 20-40, 42-47, 57, 58, 61, 62, and 65 are directed to an invention not patentably distinct from claims 20-58, 60, 62, 71, and 74-84 of commonly assigned U.S. Patent No. 6,919,307. Specifically, see the above obviousness-type double patenting rejection.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302).

Commonly assigned copending Application No. 10/138,935, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

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A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

20. Claims 2-6, 20-40, 42-47, 57-59, 61-63, and 65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 74-132 of copending Application No. 10/962,333. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '333 application anticipate the instant claims. Note that a process of using a compound anticipates claims drawn to the compound per se.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

21. Instant claims 1-19, 41, 48-57, and 62-65 are not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application 09/972,772 because the parent application, under the test of 35 U.S.C. 112, first paragraph, does not disclose compounds having the full scope of Formula I, including the  $(X)_n\text{-CR}_3\text{R}_4$  group; does not disclose compounds in which Z is alkylene, O, or  $\text{NR}_8$ ; does not disclose compounds in which P is  $\text{OR}_5$  in which  $\text{R}_5$  is other than hydrogen or alkyl; does not disclose compounds in which P is  $\text{N}(\text{R}_6)\text{R}_7$  in which  $\text{R}_6$  or  $\text{R}_7$  are other than hydrogen or alkyl or in which neither of  $\text{R}_6$  and  $\text{R}_7$  is hydrogen; does not disclose compounds in which P is alkyl; does not disclose the P groups of instant claim 19; does not disclose the specific A group of claims 41 and 48; and does not disclose the specific compounds of claim 57 beginning at page 81, line 40, and continuing through page 82, line 22.

Claims 20-40, 42-47, 56 and 58-61 are deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent applications 09/972,772 and 09/704,251 because the parent applications, under the test of 35 U.S.C. 112, first paragraph, disclose the claimed invention (see originally-filed claims 1-37 and 39-42 in the '772 application, and originally-filed claims 1-37 and 39-42 in the '251 application).

Because U.S. Patent No. 6,548,477, which issued based upon parent application 09/704,251, has a different inventorship than the instant application and has an earlier effective filing date than claims 1-19, 41, 48-57, and 62-65 of the instant application, the '477 patent is available as prior art against instant claims 1-19, 41, 48-57, and 62-65 under 35 U.S.C. 102(e).

Because U.S. Patent Application Publication 2002/0193298, which is the published version of parent application 09/972,772, has a different inventorship than the instant application and has an earlier effective filing date than claims 1-19, 41, 48-57, and 62-65 of the instant application, the '298 published application is available as prior art against instant claims 1-19, 41, 48-57, and 62-65 under 35 U.S.C. 102(e).

22. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

23. Claims 2-6, 57, and 62-65 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,548,477. See the above obviousness-type double patenting rejection. Also, e.g., the compounds prepared in Examples 13-15 of the '477 patent are the same as the first three compounds recited in instant claim 57.

24. Claims 2-6, 57, and 62-65 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication 2002/0193298. The U.S. Patent Application Publication

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'298 is the published equivalent of copending Application No. 09/972,772, applied in the provisional obviousness-type double patenting rejection set forth in section 16 above, and anticipates the claims for the same reasons. Also, e.g., the compounds prepared in Examples 13-15 of the '298 patent application publication are the same as the first three compounds recited in instant claim 57.

25. Claims 62 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Folkman et al (U.S. Patent No. 6,017,954). Folkman et al teaches a compound in Example 28 (see also the Table at column 13) which is used to treat angiogenic diseases, including rheumatism and psoriasis. Patients can be human, and administration can be oral or by injection. See, e.g., column 12, lines 8-46. The compound of Example 28 corresponds to Applicants' compound of Formula I in which A is fumagillol; W is O; R<sub>1</sub>, R<sub>3</sub>, and R<sub>4</sub> are hydrogen; either X is methylene, n=1, Z is methylene, P is N(R<sub>6</sub>)R<sub>7</sub>, and R<sub>6</sub> and R<sub>7</sub> are methyl, or n=0, Z is ethylene, P is N(R<sub>6</sub>)R<sub>7</sub>, and R<sub>6</sub> and R<sub>7</sub> are methyl.

26. Claim 64 is rejected under 35 U.S.C. 103(a) as being obvious over Folkman et al (U.S. Patent No. 6,017,954) as applied against claims 62 and 63, and further in view of Yanai et al (U.S. Patent No. 5,422,363) or Folkman et al (U.S. Patent No. 6,086,865). Folkman et al '954 teaches that the compounds can be administered to treat angiogenic diseases, but do not specifically teach treatment of rheumatoid arthritis. Yanai et al teach the administration of fumagillol derivatives to treat diseases associated with angiogenesis, such as rheumatoid arthritis. See, e.g., column 9, lines 15-18 and 51-56. Folkman et al '865 teaches the administration of fumagillol derivatives to treat angiogenesis-induced diseases, such as rheumatoid arthritis. See, e.g., column 3, lines 11-15, and column 6, lines 17-20. It would have

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been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the compounds of Folkman et al '954 so as to treat rheumatoid arthritis, because the compounds of Folkman et al '954 are disclosed to be useful in treating angiogenic diseases in general, and because Yanai et al and Folkman et al '865 teach that rheumatoid arthritis is an angiogenic disease treatable by similar fumagillol derivatives.

27. Applicant's arguments filed June 20, 2005 have been fully considered but they are not persuasive.

The double patenting rejection of claims 23, 24, and 58-61 over U.S. Patent No. 6,548,477 is maintained. Applicants' amendment to claim 23 had no effect on the scope of claim 23, because even in the originally-filed claim, Q was not permitted to be hydrogen. With respect to claims 58-61, note that the limitation "when P is hydrogen, Q is not hydrogen" also occurs at claim 58, lines 18-19. The double patenting rejection of claims 28 and 29 is withdrawn in view of the amendment to claim 20 further defining the N-terminus of the peptide. The double patenting rejection of claims 49 and 50 over U.S. Patent No. 6,548,477 is withdrawn in view of Applicants' amendment to the structural formula in independent claim 48.

Applicants did not respond to any of the requirements made in the previous Office action to show common ownership or name the prior inventors. These requirements are repeated above.

The rejection of certain of the claims under 35 U.S.C. 102(e) over U.S. Patent No. 6,548,477 and over U.S. Patent Application Publication 2002/0193298 is maintained. Applicants point to amendments made to the definitions of the variables  $R_3$  and  $R_4$  in claim 1 as establishing a patentable difference over the two references. The examiner agrees. However, it should be

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noted that the amendments made to claim 1 are not reflected in dependent claims 2-6 (see also the objection set forth in section 8 above), and no such amendments were made to claims 57 or 62. Accordingly, these claims remain rejected over U.S. Patent No. 6,548,477 and over U.S. Patent Application Publication 2002/0193298.

Claims 1, 7, and 8 are no longer rejected over Folkman et al (U.S. Patent No. 6,017,954) in view of Applicants' amendment to claim 1 deleting 'hydrogen' from the definition of R<sub>3</sub> and R<sub>4</sub>. Claims 62-64 continue to be rejected over Folkman et al as the primary reference, albeit on slightly different grounds than in the first Office action. Note that Applicants have not limited the definition of R<sub>3</sub> and R<sub>4</sub> in claim 62, have broadened the definition of Z at line 15, and permit P to be other than hydrogen or a peptide at line 17.

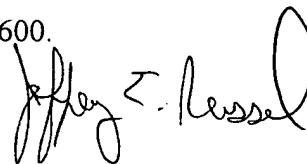
28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP §706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

A handwritten signature in black ink, appearing to read "Jeffrey E. Russel". The signature is stylized with a large, looped "J" and "R".

Jeffrey E. Russel

Primary Patent Examiner

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JRussel

July 21, 2005